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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,986	08/17/2000	Gregor Cevc	500.1011	9461

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,986	CEVC, GREGOR	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *199-224* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *199-224* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12-6.2000 7-30-04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 9-27-05 is acknowledged.

Claims included in the prosecution are 199-224.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 199-224 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation, "wherein the substrate and the at least one third substance do not have opposite charges" now introduced in claim 199 does not appear to have support in the specification as originally filed and therefore, deemed to be new matter.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 199-224 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear from claim 199 as to what the liquid medium is. Since the compositions are bilayer structures, one would assume the liquid medium to be an aqueous medium. However, claim 199 also recites the limitation that the second substance is more soluble in the liquid medium than the first substance. However, phospholipids which form the bilayer are not soluble in water, but insoluble.

Upon consideration, the 102 rejection of claims over WO and 103 rejection of the claims over WO and Uster are withdrawn.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 199-208 and 213-220 are rejected under 35 U.S.C. 102(b) as being anticipated by Weder (4,731,210).

Weder discloses compositions containing an amphipathic phospholipid, an amphipathic surfactant (cholic aid and salts) and an active agent, which is an antibody or a hormone (calcitonin and steroidal hormones). The phospholipids include lecithin,

phosphatidic acid and others. The process involves mixing the phospholipid and the solubilizing agent (sodium cholate) and adding the antibody, which is absorbed on the surface of the liposome (abstract, col. 8, line 35 through col. 9, line 67, Examples and claims, claim 4 in particular).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant in essence argues that the systems disclosed by Weder are not based on a combination of bilayer-forming substances and solubilizing substances, but on the removal of the solubilizing agent, which leads to the desired compositions. These arguments are not persuasive. First of all, applicant is incorrect in stating that the solubilizing agent is removed in Weder. Weder teaches the appropriate amounts of the lipid and the solubilizing agent for the formation of liposomes, which could be achieved by dilution or dialysis, or adding the appropriate amounts. In examples 3 and 5 on col. 14 the solubilizing agent is not removed at all. Secondly, claims 199-214 are composition claims, though recited as product by process claims and applicant has not shown that the product of Weder is different from instant product. With regard to the process claims, first of all, instant claim language does not exclude the dilution of the solubilization agent. Secondly, as pointed out above, Weder teaches that a certain ratio of the lipid and solubilizing agents are necessary to obtain the liposomes. Applicant's arguments that Weder does not teach or suggest the association/adsorption of the pharmaceutical substances are not persuasive since claim 4 in Weder clearly teaches that the pharmaceutical substance is absorbed by incubating the liposome with one pharmaceutical substance.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 199-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder (4,731,210) by itself or in combination with WO 92/03122 cited above.

As pointed out above, Weder discloses compositions containing an amphipathic phospholipid, an amphipathic surfactant (cholic aid and salts) and an active agent, which is an antibody. The process involves mixing the phospholipid and the solubilizing agent (sodium cholate) and adding the antibody, which is absorbed on the surface of the liposome (abstract, col. 8, line 35 through col. 9, line 67, Examples and claims, claim 4 in particular). Weder does not specifically disclose claimed insulin or interleukin. However, since Weder provides guidance through examples as to how to absorb the active agent on the surface of the liposome and is suggestive of the applicability of the method to proteins, it would have been obvious to one of ordinary skill in the art to use claimed insulin or interleukin with a reasonable expectation of success. One of ordinary skill in the art would be motivated further to use these active agents since the reference

of WO which teaches similar compositions is suggestive of the feasibility of the use of insulin.

Applicant's arguments have been fully considered, but are not persuasive. Applicant once again argues that the solubilizing agent is removed in Weder and that Weder does not teach the association/absorption of the substance to the surface of the liposomes. These arguments have been addressed above. Applicant argues that WO 02 does not teach or suggest the association of the macromolecules with the outside of the surface of the vesicles. These arguments are not persuasive since WO is combined for its teachings of insulin and interleukin and as pointed out above, it would have been obvious to one of ordinary skill in the art to use these substances in Weder if compositions containing these active agents are desired.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 199-224 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31, 38 and 70-76

of copending Application No. 09/621,574. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both applications are drawn to the same compositions and the ratios of the lipid to the surfactant recited in the claims of said copending application fall within the generic terms in instant claims. The species of specific active agents recited in instant claims are deemed to be anticipated by the generic term, active agent in the claims of said copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that the claims in 09/621,574 are directed to a preparation suitable for transporting active agents through permeability barriers unlike the present claims. These arguments are not persuasive since the claims recite the same components and method of preparation and the claims read on each other.

11. Claims 199-224 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-66, 80-81, 88-100 of copending Application No. 10/357,618. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both applications are drawn to the same compositions and instant species of active substances are deemed to be anticipated by the generic active ingredient recited in the claims of said patent. 'container', 'package' in which the compositions are placed as

recited in claims 80, 81 and others recited in the copending application are deemed to be obvious forms for the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the claims in the copending application are directed to preparation for application, administration or transport of an active ingredient into and through the pores in semi-permeable barriers or other constrictions and the preparation is in the form of mixed amphipat aggregates with extended surfaces and formed from the combination of at least one first amphipathic component, at least one second amphipathic component (membrane destabilizing component) and at least one third (membrane destabilizing component) amphipathic component suspended in a suitable liquid medium and the present claims are distinguishable over those in 10/357,618 and that the claims in said copending application do not teach or suggest a substrate in the form of a bilayer surface formed by at least one first surface-building amphipathic substance and at least one second surface-destabilizing amphipathic substance and molecules of at least one third amphipathic substance associated with the substrate. These arguments are not persuasive since just like in instant claims, the claims in said copending application requires three components, one is a phospholipid, the second is a surfactant and the third is an active substance and the composition is in the form of a bilayer structure. As evident from claims 64 and 67 of said copending application, the

third substance is a hormone and the drug is mainly associated with the droplet surface. The claims read on each other, and the rejection is maintained.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK